



## Complete Summary

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### GUIDELINE TITLE

Ophthalmologic complications of HIV infection.

### BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Ophthalmologic complications of HIV infection. New York (NY): New York State Department of Health; 2004 Jan. 14 p. [17 references]

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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METHODOLOGY - including Rating Scheme and Cost Analysis  
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## SCOPE

### DISEASE/CONDITION(S)

Ophthalmologic complications of human immunodeficiency virus (HIV) infection:

- Anterior segment complications including herpes zoster ophthalmicus, Kaposi's sarcoma of the lids and/or conjunctiva, microsporidia, molluscum contagiosum, and anterior uveitis
- Neuro-ophthalmic complications of HIV infection
- Retinal and choroidal manifestation of HIV infection:
  - HIV-related retinal microangiopathy
  - Infectious retinitis and choroiditis including cytomegalovirus (CMV) retinitis, progressive outer retinal necrosis, ocular toxoplasmosis, *Pneumocystis carinii* choroidopathy, and syphilis

### GUIDELINE CATEGORY

Diagnosis  
Evaluation  
Management  
Treatment

## **CLINICAL SPECIALTY**

Allergy and Immunology  
Family Practice  
Infectious Diseases  
Internal Medicine  
Ophthalmology

## **INTENDED USERS**

Advanced Practice Nurses  
Health Care Providers  
Nurses  
Physician Assistants  
Physicians  
Public Health Departments

## **GUIDELINE OBJECTIVE(S)**

To provide guidelines for diagnosis and management of ophthalmologic complications of human immunodeficiency virus (HIV) infection

## **TARGET POPULATION**

Human immunodeficiency virus (HIV)-infected patients with ophthalmologic complications

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Management of Cytomegalovirus (CMV) Retinitis**

1. Retinal examination including ophthalmoscopy
2. Referral to ophthalmologist
3. Initiating highly active antiretroviral therapy (HAART) in antiretroviral (ARV)-naïve patients and re-evaluating ARV regimen in patients receiving HAART
4. Valganciclovir induction and maintenance if retinitis is not sight-threatening
5. Treatment of sight-threatening retinitis when immune reconstitution is likely: intravenous ganciclovir or foscarnet plus valganciclovir
6. Treatment of sight-threatening retinitis when immune reconstitution is unlikely: combination of local and parenteral therapy plus ganciclovir implant plus valganciclovir
7. Monitoring for progression or reactivation of CMV retinitis by examination and serial retinal photography
8. Prophylaxis with oral ganciclovir and regular evaluations by ophthalmologist

### **Management of Other Ophthalmologic Complications**

1. Referral to ophthalmologist
2. Intravenous acyclovir followed by oral valganciclovir for herpes zoster ophthalmicus
3. For ocular toxoplasmosis: central nervous system evaluation; same treatment as that for central nervous system toxoplasmosis (e.g., sulfadiazine, pyrimethamine, and leucovorin); alternative treatment: atovaquone and/or azithromycin; maintenance therapy to prevent relapse
4. Standard anti-pneumocystis therapy (e.g., trimethoprim/sulfamethoxazole) for *Pneumocystis carinii* choroidopathy
5. Intravenous penicillin G for syphilitic uveitis, chorioretinitis, or optic nerve disease

## **MAJOR OUTCOMES CONSIDERED**

Efficacy and safety of treatment

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

Not stated

### **NUMBER OF SOURCE DOCUMENTS**

Not stated

### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Expert Consensus (Committee)

### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

Not applicable

### **METHODS USED TO ANALYZE THE EVIDENCE**

Review

### **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

### **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with HIV infection. Committees\* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees\* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

\* Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Committee
- Women's Health Committee
- Substance Use Committee
- Physician's Prevention Advisory Committee
- Pharmacy Committee

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

Not applicable

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

# **RECOMMENDATIONS**

## **MAJOR RECOMMENDATIONS**

Patients with CD4 counts  $<50$  cells/mm<sup>3</sup> should be examined by an ophthalmologist every 6 months. (Kuppermann et al., 1993; Whitly et al., 1998)

Patients with visual disturbances or unremitting ocular symptoms, regardless of CD4 cell count, should be evaluated by an ophthalmologist. The severity of signs and symptoms should guide the clinician in choosing whether to request emergency consultation.

Retinal examination in human immunodeficiency virus (HIV)-infected patients should include indirect ophthalmoscopy through a dilated pupil so the entire peripheral fundus can be evaluated.

The primary care clinician and the ophthalmologist should work in conjunction to manage ocular opportunistic infections in HIV-infected patients.

### **Anterior Segment Complications of HIV**

#### **Herpes Zoster Ophthalmicus**

The clinician should refer patients with herpes zoster ophthalmicus for evaluation by an ophthalmologist because uveitis, corneal opacities, or secondary glaucoma may develop. The retina should also be examined because the infection can involve the posterior segment as well, which is a medical emergency. See below: *Infectious Retinitis and Choroiditis* for information on zoster retinitis (progressive outer retinal necrosis).

#### *Treatment*

Clinicians should treat HIV-infected patients with herpes zoster ophthalmicus with intravenous acyclovir (10 mg/kg) every 8 hours for 10 to 14 days. It should be administered at a constant rate for 1 hour to prevent renal tubular damage. The course of intravenous acyclovir should be followed by oral therapy with valganciclovir (1 g three times a day [tid]) until lesions have healed.

### **Neuro-Ophthalmic Complications of HIV**

Patients with orbital and central nervous system opportunistic infections and malignancies should undergo neurologic evaluation, neuroimaging studies, and further evaluation by specialists.

Refer to Table 1 in the original guideline document for the list of ocular disturbances associated with orbital and central nervous system opportunistic infections, as well as which guideline to refer to for recommendations concerning diagnosis and treatment.

### **Retinal and Choroidal Manifestations of HIV Infection**

#### **HIV-Related Retinal Microangiopathy**

#### *Diagnosis*

Patients who are suspected of having retinal microangiopathy but have visual complaints should be re-evaluated serially to exclude an alternative diagnosis.

## **Infectious Retinitis and Choroiditis**

The primary care clinician and the ophthalmologist should work in conjunction to manage infectious retinitis and choroiditis in HIV-infected patients.

### *Cytomegalovirus (CMV) Retinitis*

#### Treatment of CMV Retinitis

Clinicians should initiate highly active antiretroviral therapy (HAART) in antiretroviral (ARV)-naïve patients who present with CMV retinitis.

When patients who are receiving HAART present with CMV retinitis, clinicians should re-evaluate the ARV regimen in an attempt to maximize the effect of HAART on the immune system. However, CMV retinitis should be treated with both HAART and specific antiviral treatment, which varies depending on the immune status of the patient (refer to Figure 1 in the original guideline document for more information).

Because the ganciclovir implant does not start consistent delivery of medication to the retina until the second week after placement, patients should receive 2 weeks of an anti-CMV agent, such as intravenous ganciclovir or oral valganciclovir, immediately following implant placement.

When systemic therapy alone is indicated:

- A 2- to 3-week induction period with one of the following should be used to stabilize CMV retinitis:
- Typical first-line therapy options:
  - Intravenous ganciclovir (5 mg/kg twice daily [bid] for 14 to 21 days, then 5 mg/kg once daily [qd] for 21 days), or
  - Oral valganciclovir (900 mg orally [PO] bid for 21 days, then 900 mg PO qd).
- Acceptable first-line therapy options in select cases (e.g., long-standing previous prophylaxis with ganciclovir):
  - Foscarnet (60 mg/kg IV every 8 hours or 90 mg/kg intravenously [IV] every 12 hours for 14 to 21 days, then 90 to 120 mg/kg IV every 12 hours), or
  - Cidofovir (5 mg/kg IV once weekly for 2 weeks, then 5 mg/kg every 2 weeks; with probenecid, 2 g PO 3 hours before each cidofovir dose, 1 g PO at 2 hours and again at 8 hours post cidofovir dose)

The clinician should base the need for all maintenance regimens on the patient's immune status. If patients have achieved immune reconstitution with a CD4 count  $>100$  cells/mm<sup>3</sup> for more than 6 months, discontinuation of maintenance therapy should be considered.

<b>Table</b> <b>Choosing the Treatment Modality for CMV Retinitis</b>	
<b>Consideration</b>	<b>Effect on Treatment Choice</b>
The location and extent of CMV retinitis (i.e., sight threatening or peripheral) and the status of the fellow eye	If the patient has sight-threatening CMV retinitis or bilateral disease, parenteral therapy should be used.
Whether the disease is newly diagnosed or relapsed	If the patient is experiencing a relapse, combination therapy with two parenteral agents has produced the best results.
The immune status of the patient	The immune status of the patient will determine whether an implant is required (see Figure 1 in the original guideline document).
Whether the patient is HAART naïve or whether HAART has failed	HAART should be initiated in naïve patients, and the regimen should be optimized in patients with failing HAART.
The presence of other conditions that can affect medication choice	For example, for patients actively using drugs, the implant may facilitate treatment.
Other medications with overlapping toxicities	Overlapping toxicities may help decide between ganciclovir versus foscarnet. For example, if a patient has neutropenia that is unlikely to resolve, ganciclovir should be avoided.
Adherence to follow-up	For patients with poor adherence, the implant may facilitate treatment.
Patient's preference and quality-of-life concerns	Quality-of-life issues may sway a patient away from parenteral therapy.

#### Reactivation or Progression of CMV Retinitis

During therapy, the ophthalmologist should monitor for progression or reactivation of retinitis by examination and serial retinal photography.

#### Prophylaxis for CMV Retinitis

Patients receiving oral ganciclovir prophylaxis or therapy for extraocular CMV should be evaluated every 3 months by an ophthalmologist because treatment may mask the development of symptoms of retinitis.

#### *Ocular Toxoplasmosis*

##### Treatment

Clinicians should perform a central nervous system evaluation in patients with ocular toxoplasmosis.

Therapy for ocular toxoplasmosis should be the same as that for central nervous system toxoplasmosis. Atovaquone and/or azithromycin can be considered for patients in whom standard therapy fails or may not be used (e.g., allergies to sulfa or clindamycin).

Clinicians should continue maintenance therapy to prevent relapse of toxoplasmosis lesions.

#### *Pneumocystis carinii* Choroidopathy

##### Treatment

Because ocular *Pneumocystis carinii* is a manifestation of disseminated pneumocystosis, clinicians should initiate standard anti-pneumocystis therapy.

#### *Syphilis*

##### Diagnosis and Treatment

Clinicians should treat patients with syphilitic uveitis, chorioretinitis, or optic nerve disease for neurosyphilis. The treatment of ocular syphilis optimally will include 2 weeks of intravenous penicillin G.

### **CLINICAL ALGORITHM(S)**

An algorithm is provided in the original guideline document for Initiation of Treatment for CMV Retinitis.

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **REFERENCES SUPPORTING THE RECOMMENDATIONS**

[References open in a new window](#)

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is not specifically stated for each recommendation.

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Appropriate diagnosis and treatment of ophthalmologic complications associated with human immunodeficiency virus (HIV) infection

### **POTENTIAL HARMS**

#### **Adverse Effects of Medications**

- *Ganciclovir*: Neutropenia, thrombocytopenia, gastrointestinal (GI) symptoms, diarrhea, nausea, anemia, development of resistance
- *Valganciclovir*: GI symptoms, neutropenia, anemia, thrombocytopenia



- *Foscarnet*: Nephrotoxicity, hypomagnesemia, hypocalcemia, hypokalemia, penile and genital ulcers in uncircumcised men receiving high doses with poor hydration prior to treatment
- *Cidofovir*: Vomiting, nausea, rash, headache, anorexia, anemia, severe uveitis, irreversible hypotony, neutropenia
- Oral ganciclovir: Neutropenia, diarrhea, anemia, thrombocytopenia
- Intraocular ganciclovir implant: Temporary loss of functional visual acuity after surgery, risk of early retinal detachment, endophthalmitis
- Fomivirsen: Ocular inflammation (uveitis, vitritis), increased intraocular pressure, pigmentary retinopathy

Refer to Table 3 in the original guideline document for more information about these drugs and their combinations.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

- *Ganciclovir* should be avoided in patients with neutropenia that is unlikely to resolve
- *Cidofovir* and *foscarnet* should be avoided in patients with renal insufficiency (creatinine clearance <55; creatinine >1.5) and should not be used concomitantly with other nephrotoxic agents.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with HIV infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

#### Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative, the AIDS Educational Training Centers (AETC) and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the NYSDOH Distribution Center for providers who lack internet access.

#### Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted

through the Clinical Education Initiative (CEI) and the AIDS Education and Training Centers (AETC). The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

## **IMPLEMENTATION TOOLS**

Clinical Algorithm  
Personal Digital Assistant (PDA) Downloads

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## **INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES**

### **IOM CARE NEED**

Getting Better  
Living with Illness

### **IOM DOMAIN**

Effectiveness

## **IDENTIFYING INFORMATION AND AVAILABILITY**

### **BIBLIOGRAPHIC SOURCE(S)**

New York State Department of Health. Ophthalmologic complications of HIV infection. New York (NY): New York State Department of Health; 2004 Jan. 14 p. [17 references]

**ADAPTATION**

Not applicable: The guideline was not adapted from another source.

**DATE RELEASED**

2004 Jan

**GUIDELINE DEVELOPER(S)**

New York State Department of Health - State/Local Government Agency [U.S.]

**SOURCE(S) OF FUNDING**

New York State Department of Health

**GUIDELINE COMMITTEE**

Not stated

**COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

Not stated

**FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Not stated

**GUIDELINE STATUS**

This is the current release of the guideline.

**GUIDELINE AVAILABILITY**

Electronic copies: Available from the [New York State Department of Health AIDS Institute Web site](#).

**AVAILABILITY OF COMPANION DOCUMENTS**

This guideline is available as a Personal Digital Assistant (PDA) download from the [New York State Department of Health AIDS Institute Web site](#).

**PATIENT RESOURCES**

None available

## **NGC STATUS**

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